

## **Exhibit 4**

**Exhibit 4 - Allowed Claims in U.S. Serial No. 10/323,314**

32. A method of inhibiting human immunodeficiency virus infection of a CD4+ cell which also carries a CCR5 receptor on its surface which comprises contacting the CD4+ cell with an amount of a binding-inhibiting compound effective to inhibit binding of human immunodeficiency virus to the CCR5 receptor so as to thereby inhibit human immunodeficiency virus infection of the CD4+ cell, said binding-inhibiting compound comprising the structure



wherein T represents a threonine, S represents a serine, E represents a glutamic acid, each Y represents a tyrosine, D represents an aspartic acid, I represents an isoleucine, and N represents an asparagine;

wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with the I at position 9 and extending therefrom in the amino terminal direction;

wherein  $\beta$  represents from 0 to 13 amino acids, with the proviso that if there are more than 2 amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with the P at position 19 and extending therefrom in the carboxy terminal direction;

wherein  $\theta$  represents an amino group or an acetylated amino group;

wherein  $\lambda$  represents a carboxyl group or an amidated carboxyl group;

wherein all of  $\alpha$ , Y, D, I, N, Y, Y, T, S, E and  $\beta$  are joined together by peptide bonds;

further provided that at least two of the tyrosines represented by Y in the YDINYYTSE portion of the structure of the compound are sulfated.

45. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:
- (a) immobilizing the binding-inhibiting compound of claim 32 on a solid support;
  - (b) contacting the immobilized compound from step (a) with sufficient detectable CCR5 ligand to saturate all binding sites for the CCR5 ligand on the immobilized compound under conditions permitting binding of the CCR5 ligand to the immobilized compound so as to form a complex;
  - (c) removing any unbound CCR5 ligand;
  - (d) contacting the complex from step (b) with the agent; and
  - (e) detecting whether any CCR5 ligand is displaced from the complex, wherein displacement of detectable CCR5 ligand from the complex indicates that the agent binds to the compound so as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.
49. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:
- (a) contacting the binding-inhibiting compound of claim 32 with the agent and detectable CCR5 ligand under conditions permitting binding of the CCR5 ligand to the compound so as to form a complex;
  - (b) removing any unbound CCR5 ligand;
  - (c) measuring the amount of detectable CCR5 ligand which is bound to the compound in the complex;

- (d) measuring the amount of detectable CCR5 ligand which binds to the compound in the absence of the agent; and
- (e) comparing the amount of CCR5 ligand which is bound to the compound in step (c) with the amount measured in step (d), wherein a reduced amount measured in step (c) indicates that the agent binds to the compound or CCR5 ligand so as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.

52. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:

- (a) immobilizing the binding-inhibiting compound of claim 32 on a solid support;
- (b) contacting the immobilized compound from step (a) with the agent dissolved or suspended in a known vehicle and measuring the binding signal generated by such contact;
- (c) contacting the immobilized compound from step (a) with a known vehicle in the absence of the compound and measuring the binding signal generated by such contact; and
- (d) comparing the binding signal measured in step (b) with the binding signal measured in step (c), wherein an increased amount measured in step (b) indicates that the agent binds to the compound so as to thereby identify the agent as one which binds to the CCR5 receptor.

55. A method of obtaining a composition which comprises:
- (a) identifying a compound which inhibits binding of a CCR5 ligand to a CCR5 receptor according to the method of claim 45: and
  - (b) admixing the compound so identified or a homolog or derivative thereof with a carrier.

64. A compound having the structure:



wherein T represents a threonine, S represents a serine, E represents a glutamic acid, each Y represents a tyrosine, D represents an aspartic acid, I represents an isoleucine, and N represents an asparagine;

wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with I at position 9 and extending therefrom in the amino terminal direction;

wherein  $\beta$  represents from 0 to 13 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with P at position 19 and extending therefrom in the carboxy terminal direction;

wherein  $\lambda$  represents a carboxyl group or an amidated carboxyl group;

wherein all of  $\alpha$ , Y, D, I, N, Y, Y, T, S, E and  $\beta$  are joined together by peptide bonds;

further provided that at least two of the tyrosines represented by Y in the YDINYYTSE structure of the compound are sulfated, and

wherein  $n$  is an integer from 1 to 8,  $\Delta$  is a polymer, and the solid line represents up to 8 linkers which attach the structure in parentheses to  $\Delta$ .

79. A composition comprising the binding-inhibiting compound of claim 32 and a detectable marker attached thereto.
80. A composition which comprises a carrier and an amount of the binding-inhibiting compound of claim 32 effective to inhibit binding of HIV-1 to a CCR5 receptor on the surface of a CD4+ cell.
82. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:
- (a) contacting the binding-inhibiting compound of claim 32 with sufficient detectable CCR5 ligand to saturate all binding sites for the CCR5 ligand on the compound under conditions permitting binding of the CCR5 ligand to the compound so as to form a complex;
  - (b) removing any unbound CCR5 ligand;
  - (c) measuring the amount of CCR5 ligand which is bound to the compound in the complex;
  - (d) contacting the complex from step (a) with the agent so as to displace CCR5 ligand from the complex;
  - (e) measuring the amount of CCR5 ligand which is bound to the compound in the presence of the agent; and
  - (f) comparing the amount of CCR5 ligand bound to the compound in step (e) with the amount measured in step (c), wherein a reduced amount measured in step (e) indicates that the agent binds to the compound so as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.

83. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:
- (a) immobilizing the binding-inhibiting compound of claim 32 on a solid support;
  - (b) contacting the immobilized compound from step (a) with the agent and detectable CCR5 ligand under conditions permitting binding of the CCR5 ligand to the immobilized compound so as to form a complex;
  - (c) removing any unbound CCR5 ligand;
  - (d) measuring the amount of detectable CCR5 ligand which is bound to the immobilized compound in the complex;
  - (e) measuring the amount of detectable CCR5 ligand which binds to the immobilized compound in the absence of the agent;
  - (f) comparing the amount of CCR5 ligand which is bound to the immobilized compound in step (e) with the amount measured in step (d), wherein a reduced amount measured in step (d) indicates that the agent binds to the compound or CCR5 ligand so as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.
84. A compound having the structure:
- $$(\theta\alpha\text{YDINYYTSE}\beta)_n-\Delta$$
- wherein T represents a threonine, S represents a serine, E represents a glutamic acid, each Y represents a tyrosine, D represents an aspartic acid, I represents an isoleucine, and N represents an asparagine;
- wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth

in SEQ ID NO:1 beginning with the I at position 9 and extending therefrom in the amino terminal direction;  
wherein  $\beta$  represents from 0 to 13 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with the P at position 19 and extending therefrom in the carboxy terminal direction;  
wherein  $\theta$  represents an amino group or an acetylated amino group;  
wherein all of  $\alpha$ , Y, D, I, N, Y, Y, T, S, E and  $\beta$  are joined together by peptide bonds,  
further provided that at least two of the tyrosines represented by Y in the YDINYYTSE structure of the compound are sulfated, and  
wherein n is an integer from 1 to 8,  $\Delta$  is a polymer, and the solid line represents up to 8 linkers which attach the structure in parentheses to  $\Delta$ .

85. A compound comprising the structure:



wherein E represents a glutamic acid, and each Y represents a tyrosine;  
wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than two amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO:1 beginning with the I at position 9 and extending therefrom in the amino terminal direction;  
wherein  $\beta$  represents from 0 to 13 amino acids, with the proviso that if there are more than 2 amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID



NO:1 beginning with the P at position 19 and extending therefrom in the carboxy terminal direction;  
wherein  $\theta$  represents an amino group or an acetylated amino group;  
wherein  $\lambda$  represents a carboxyl group or an amidated carboxyl group;  
wherein  $\pi$  represents any amino acid;  
wherein all of  $\alpha$ , Y, D,  $\pi$ ,  $\pi$ , Y,  $\pi$ ,  $\pi$ ,  $\pi$ , E and  $\beta$  are joined together by peptide bonds; and  
further provided that the two tyrosines represented by Y in the YD $\pi\pi$ Y $\pi\pi\pi$ E structure of the compound are sulfated.